WILMS' TUMOUR—SOME OBSERVATIONS AND RESULTS OF TREATMENT AT THE NORTHERN IRELAND RADIOTHERAPY CENTRE, 1953-1959

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In the group of serious diseases occurring in childhood it is fortunate that Wilms' tumour is uncommon. It is of insidious onset, treatment is not satisfactory and it is often at a late stage when the clinician sees it for the first time. Early diagnosis is unlikely and most patients are brought to hospital because of a large swelling in one or other side of the abdomen. The tumour may be a neuroblastoma of the adrenal gland, a renal cyst, a retroperitoneal tumour, congenital hydronephrosis or similar rare abnormality, as well as Wilms' tumour, while enlargement of the spleen and liver may also have to be considered. Retrograde or intravenous pyelography may prove helpful in diagnosis, but almost always the diagnosis is uncertain until after laparotomy and biopsy.

Wilms' tumours are often large when first seen and this increases the liability to trauma with the risk of hæmorrhage into the tumour or rupture. A large tumour is more radio-resistant than a smaller one, though the tumours can often be greatly reduced in size with pre-operative radiation even when quite enormous. Handling of the child's abdomen should be reduced to a minimum since pressure may well expel tumour cells into the radicles of the renal vein and allow metastases to reach the lungs more easily. This does not necessarily herald a fatal outcome as evidenced by one of our cases below.

Histology.

Willis (1953) and others have given excellent descriptions of the cellular structure of these tumours. Enormous variations of cell type occur; innate ability to disseminate and the degree of radiosensitivity of the malignant tissues will determine the outcome but cannot be predicted.

Treatment.

For obvious reasons in tumours occurring commonly methods of treatment are likely to be established on a firm basis. In the case of Wilms' tumour considerable difference of opinion persists about some of the methods of control. Many authors have only small series of cases, e.g., thirty-eight cases occurred at the Boston Children's Hospital between 1940 and 1947. Only fifteen cases in Belfast have been referred to the Radiotherapy Centre since 1953 and as five of these are so recent an assessment can only be made in ten cases. The following methods of treatment are used:

1. *Surgery.*

Nephrectomy alone is used by some as the method of treatment. Ladd and White (1941) published a report of a series of 64 cases with 14 survivors. Harvey

(1950) reported 28 patients out of 180 surviving at two years. Surgery alone is not now considered to give the best results.

2. *Radiation only.*

While this method of treatment appears to have been used with success in some patients, and must be used in very advanced inoperable cases if any therapy is to be attempted at all, it is not justified by results. Dean (1945) reported 5 out of 20 patients who did well, and cures in occasional patients have been reported by authors such as Nesbitt and Adams (1946).

3. *Pre-operative Radiation followed by Surgery.*

This method of treatment has in recent years come into disfavour following the comments of Gross (1953) and the Boston School. Its supporters recommend it on the grounds that it may make surgery easier and thereby lessens the risk of dissemination of the tumour in addition to reducing or abolishing its malignancy. While these arguments may carry some weight, this method has disadvantages: —

(a) It delays the removal of the primary tumour, the source of disseminating cells.

(b) The tumour may be resistant to radiation.

(c) If the tumour disappears the parent of the child may refuse operation and no histological proof of disease be obtained.

4. *Surgery plus Post-operative Radiation.*

This method may seem irrational if one believed the disease to be confined to the kidney and to spread by the veins but the tumour may also spread by lymphatics and the lymphatics adjacent to the renal vein and along the para aortic lymph channels may become involved. In addition it is possible that contamination of the tissues adjacent to the renal pedicle by tumour cells may take place particularly if a tumour capsule ruptures at operation.

Gross (1953) reported very good results in his survey of cases treated between 1940 and 1947. There were eighteen two-year survivals among 38 cases. Warnings by other authors about assessing this time as a period of cure are given and many late recurrences have been reported.

5. *Surgery and Pre- and Post-operative Radiation.*

Gross (1959) commented favourably on this method. There can be little doubt that individual decisions about treatment methods are often needed, and it is not always possible to define a policy which can be attached to a whole group of patients. The present position appears to be that post-operative radiation is desirable either with or without pre-operative radiation.

Abeshouse (1957) examined 212 cases from the literature who had pre- and post-operative radiation. These had a two-year cure rate of 31 per cent. He compared them with another group who had post-operative radiation only and a survival rate of 28 per cent. Such a difference is quite insignificant statistically.

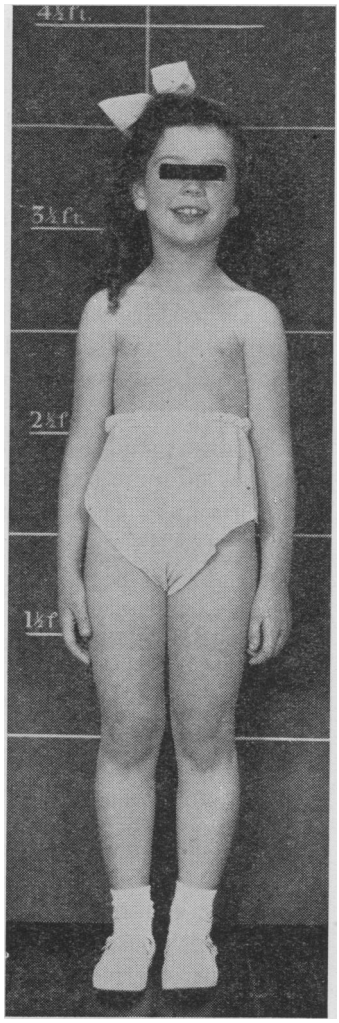
Cases Treated at Northern Ireland Radiotherapy Centre.

The results in the ten assessable cases at this Centre can be tabulated as follows. The series is of interest, containing a child who has survived over five years having been treated for pulmonary metastases.

Age	Description of Tumour	Radiation	Result
1. c.8/12.	6 cm. in diameter.	Post-operative; 2500r in 17 days.	Recurr. in 5/12. Died in 6/12.
2. 1 year.	Large tumour adherent to liver.	Post-operative; 1584r in 27 days.	Recurr in 2/12. Died in 4/12.
3. 1 year.	Large necrotic tumour. Capsule broke. Metastases in mesentery.	Too ill.	Died 1/12 later.
4. 5.10/12.	Large soft tumour with ruptured capsule.	Post-operative; 1730r in 20 days.	Recurr. in 9/12. Died in 12/12.
5. 5½ years.	5 cm. tumour. Capsule not ruptured.	Pre-operative; 2600r in 33 days. Little reduction in size.	Well 4½ years.
6. 2 years.	10 x 8 cm. tumour.	Post-operative. Chest metastases successfully treated (see below).	Well 5½ years.
7. 1 year.	12 x 8 x 9 cm. (700 gm.).	Post-operative; 2500r in 28 days.	Well 3½ years later.
8. 6.6/12.	"Turnip-sized tumour."	Post-operative; 1360r in 13 days to whole abdomen; 1925r to L. side in 28 days subsequently.	Recurr. in 2/12. Died in 8/12.
9. 6.10/12.	8 cm. tumour.	Pre-operative; 3500r in 20 days; 20 x 15 cm. fields to R. renal region. Chest metastases 6/52 later; 2300r in 41 days to whole chest.	Recurr. in 6/52 and died 9/12 later.
*10. 8.6/12.	Large mass in abdomen with chest metastases when first seen.	Whole upper half abdomen and whole chest.	No evidence metastases 8/12 later. To date.

*Case 10 was not proven histologically and received radiation only.

There are few cases with chest metastases which have survived. They have been described by Kerr (1939), Nesbitt and Adams (1946), Silver (1947), and Ng. and Low Beer (1956). Such survival confirms the radiosensitive nature of some of these tumours. The case of the child listed as No. 6 is of interest, and is briefly outlined below.



Case 6.

She was first seen at the Royal Belfast Hospital for Sick Children by Mr. Ian Fraser in August, 1953; she was 2 years old. There was a swelling in the right loin which suggested Wilm's tumour. Two days later operation was undertaken. A tumour 10 x 8 cm. in size was found in the upper pole of the right kidney. Removal appeared to be complete. Histology confirmed the diagnosis. An X-ray of chest before operation and on 10.9.53 was negative. She was subsequently referred for radiation and X-ray therapy to the right renal region was given between 15.9.53 and 5.10.54. The maximum tissue dose was 2,500r at 230 KV.

In March, 1954, there was a tiny area of opacity noted in the right upper lung field. It was not certain that this was a pulmonary metastasis until three months later, and the slow rate of growth of the tumour is of interest. As the patient's general condition was very good it was decided to irradiate the whole chest. 2070r in twenty days was given between 20.7.54 and 10.8.54. A film of the chest on 16.9.54 was negative. The present appearance of the chest film is satisfactory. The child has been in excellent health since. She presents no evidence of any pulmonary fibrosis and has a normal exercise tolerance test. Her height is normal and as in the other areas no evidence of interference with growth has been noted (see figure).

Comment.

It is gratifying that four out of ten patients have made a good response to treatment and probably three of them can be regarded as cured. Six patients are failures. All these died in one year or less after therapy. In two of them it will be noted that the capsule of the tumour had either ruptured or that the tumour presented with bad prognostic findings such as being very large and in one case was adherent to the liver. In another of the patients showing rupture there were metastatic deposits in the mesentery.

The three patients with a good result have all survived over three years, but there are reports of pulmonary metastases occurring after four years. The prognosis in children under 12 months is considerably better than in the older child.

Hypertension has not been described in any of our patients and it is not present in survivors. It is important as far as possible to protect the normal kidney from radiation. Radiation of the total renal substance may later induce a raised blood pressure.

In an attempt to derive knowledge from the follow-up of a large number of tumours Abeshouse has examined reports of 256 cases and this large group provides some interesting findings showing that bilateral involvement of the adrenal substance occurred in 12 (1.4 per cent.) of patients. The bilateral involvement is not unexpected as the disease is considered to have its origin in a developmental defect. Even such bilateral involvement may not mean a hopeless prognosis as Gross describes a child who, treated by radiation only to the abdomen and with prophylactic irradiation of the chest to low dosage of 600r, has survived for twelve years. The two-year cure rate was of the order of 30 per cent.

Abeshouse's study also showed that both kidneys could be affected equally and there was no increased tendency in either sex. Familial occurrence was not seen in this group of cases, though it has been reported by Maslow Chapian (1948), De Vries (1954), and a few other authors.

Ng. and Low Beer produce results of a carefully compiled group of twenty-seven cases who were treated by various methods. They received pre- and post-operative radiation but again the series is small and inconclusive.

Procedure for Treatment.

The following is suggested:—

1. Handling of the child's abdomen should be reduced to a minimum.
2. In children with large but operable tumours pre-operative radiation should be given with the intention of reducing the tumour size, rendering surgery easier and reducing the risk of capsule rupture. Post-operative radiation should be used as well even in the uncomplicated cases. If chest metastases are present radiation is likely to be the only hope of control.
3. In tumours which are smaller and in whom the surgeon feels that operation can be undertaken immediately, pre-operative radiation only delays the removal of the primary tumour. Post-operative radiation should be started immediately after surgery.
4. The rare bilateral tumours are probably best treated by radiation.
5. Rarely metastases in the chest may be treated successfully especially in cases with slow tumour evolution.

6. It is possible that intensive chemotherapy with some of the radiomimetic drugs may be able to palliate successfully certain types of metastatic lesion. No cures with this type of therapy have been reported.

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